



SEQUENCE LISTING

<110> Galdes, Alphonse
Mahanthappa, Nagesh

<120> METHODS AND COMPOSITIONS FOR TREATING OR PREVENTING
PERIPHERAL NEUROPATHIES

<130> CIBT-P02-052

<140> 09/435,733

<141> 1999-11-08

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<170> PatentIn Ver. 2.0

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Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly			
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Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg	
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Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala	
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Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser	
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Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn	
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Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg	

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Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr	
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Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp	
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Trp	Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	
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Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu	
355 360 365	

gcg cac gcg ctg ctg gcc gcg ctg gca ccc gcc cgc acg gac ggc ggg	1152
Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly	
370 375 380	

ggc ggg ggc agc atc cct gca gcg caa tct gca acg gaa gcg agg ggc	1200
Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly	
385 390 395 400	

gcg gag ccg act gcg ggc atc cac tgg tac tcg cag ctg ctc tac cac	1248
Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His	
405 410 415	

att ggc acc tgg ctg ttg gac agc gag acc atg cat ccc ttg gga atg	1296
Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met	
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Ala Val Lys Ser Ser	
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 <213> zebrafish Shh

<220>
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 <222> (1)..(1254)

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Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser	
1 5 10 15	

ttg gtg gtg tcc gga ctg gcc tgc ggt cct ggc aga ggc tac ggc aga	96
Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg	
20 25 30	

aga aga cat ccg aag aag ctg aca cct ctc gcc tac aag cag ttc ata	144
Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile	
35 40 45	

cct aat gtc gcg gag aag acc tta ggg gcc agc ggc aga tac gag ggc	192
Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly	
50 55 60	

aag ata acg cgc aat tcg gag aga ttt aaa gaa ctt act cca aat tac	240
Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr	
65 70 75 80	

aat ccc gac att atc ttt aag gat gag gag aac acg gga gcg gac agg	288
Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg	
85 90 95	
ctc atg aca cag aga tgc aaa gac aag ctg aac tcg ctg gcc atc tct	336
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser	
100 105 110	
gta atg aac cac tgg cca ggg gtt aag ctg cgt gtg aca gag ggc tgg	384
Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp	
115 120 125	
gat gag gac ggt cac cat ttt gaa gaa tca ctc cac tac gag gga aga	432
Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg	
130 135 140	
gct gtt gat att acc acc tct gac cga gac aag agc aaa tac ggg aca	480
Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr	
145 150 155 160	
ctg tct cgc cta gct gtg gag gct gga ttt gac tgg gtc tat tac gag	528
Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu	
165 170 175	
tcc aaa gcc cac att cat tgc tct gtc aaa gca gaa aat tcg gtt gct	576
Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala	
180 185 190	
gcg aaa tct ggg ggc tgt ttc cca ggt tcg gct ctg gtc tcg ctc cag	624
Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln	
195 200 205	
gac gga gga cag aag gcc gtg aag gac ctg aac ccc gga gac aag gtg	672
Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val	
210 215 220	
ctg gcg gca gac agc gcg gga aac ctg gtg ttc agc gac ttc atc atg	720
Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met	
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ttc aca gac cga gac tcc acg acg cga cgt gtg ttt tac gtc ata gaa	768
Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu	
245 250 255	
acg caa gaa ccc gtt gaa aag atc acc ctc acc gcc gct cac ctc ctt	816
Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu	
260 265 270	
ttt gtc ctc gac aac tca acg gaa gat ctc cac acc atg acc gcc gcg	864
Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala	
275 280 285	
tat gcc agc agt gtc aga gcc gga caa aag gtg atg gtt gtt gat gat	912
Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp	
290 295 300	

agc ggt cag ctt aaa tct gtc atc gtg cag cgg ata tac acg gag gag	960
Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu	
305 310 315 320	

cag cgg ggc tcg ttc gca cca gtg act gca cat ggg acc att gtg gtc	1008
Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val	
325 330 335	

gac aga ata ctg gcg tcc tgt tac gcc gta ata gag gac cag ggg ctt	1056
Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu	
340 345 350	

gcg cat ttg gcc ttc gcg ccc gcc agg ctc tat tat tac gtg tca tca	1104
Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser	
355 360 365	

ttc ctg tcc ccc aaa act cca gca gtc ggt cca atg cga ctt tac aac	1152
Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn	
370 375 380	

agg agg ggg tcc act ggt act cca ggc tcc tgt cat caa atg gga acg	1200
Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr	
385 390 395 400	

tgg ctt ttg gac agc aac atg ctt cat cct ttg ggg atg tca gta aac	1248
Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn	
405 410 415	

tca agc tg	1256
Ser Ser	

<210> 6
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 <213> human Shh

<220>
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 <222> (1)..(1425)

<220>
 <223> "nnn" encoding "Xaa" at position 1387-1389 may be a, t, c, g, other or unknown

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1 5 10 15	

ctg gta tgc tcg gga ctg gcg tgc gga ccg ggc agg ggg ttc ggg aag	96
Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys	
20 25 30	

agg agg cac ccc aaa aag ctg acc cct tta gcc tac aag cag ttt atc	144
Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile	
35 40 45	

ccc aat gtg gcc gag aag acc cta ggc gcc agc gga agg tat gaa ggg	192
Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly	
50 55 60	
aag atc tcc aga aac tcc gag cga ttt aag gaa ctc acc ccc aat tac	240
Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr	
65 70 75 80	
aac ccc gac atc ata ttt aag gat gaa gaa aac acc gga gcg gac agg	288
Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg	
85 90 95	
ctg atg act cag agg tgt aag gac aag ttg aac gct ttg gcc atc tcg	336
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser	
100 105 110	
gtg atg aac cag tgg cca gga gtg aaa ctg cgg gtg acc gag ggc tgg	384
Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp	
115 120 125	
gac gaa gat ggc cac cac tca gag gag tct ctg cac tac gag ggc cgc	432
Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg	
130 135 140	
gca gtg gac atc acc acg tct gac cgc gac cgc agc aag tac ggc atg	480
Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met	
145 150 155 160	
ctg gcc cgc ctg gcg gtg gag gcc ggc ttc gac tgg gtg tac tac gag	528
Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu	
165 170 175	
tcc aag gca cat atc cac tgc tcg gtg aaa gca gag aac tcg gtg gcg	576
Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala	
180 185 190	
gcc aaa tcg gga ggc tgc ttc ccg ggc tcg gcc acg gtg cac ctg gag	624
Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu	
195 200 205	
cag ggc ggc acc aag ctg gtg aag gac ctg agc ccc ggg gac cgc gtg	672
Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val	
210 215 220	
ctg gcg gcg gac gac cag ggc cgg ctg ctc tac agc gac ttc ctc act	720
Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr	
225 230 235 240	
ttc ctg gac cgc gac gac ggc gcc aag aag gtc ttc tac gtg atc gag	768
Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu	
245 250 255	
acg cgg gag ccg cgc gag cgc ctg ctg ctc acc gcc gcg cac ctg ctc	816
Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu	
260 265 270	
ttt gtg gcg ccg cac aac gac tcg gcc acc ggg gag ccc gag gcg tcc	864

Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Ala	Thr	Gly	Glu	Pro	Glu	Ala	Ser		
		275					280					285					
tcg	ggc	tcg	ggg	ccg	cct	tcc	ggg	ggc	gca	ctg	ggg	cct	cgg	gcg	ctg	912	
Ser	Gly	Ser	Gly	Pro	Pro	Ser	Gly	Gly	Ala	Leu	Gly	Pro	Arg	Ala	Leu		
	290					295					300						
ttc	gcc	agc	cgc	gtg	cgc	ccg	ggc	cag	cgc	gtg	tac	gtg	gtg	gcc	gag	960	
Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val	Ala	Glu		
305					310					315					320		
cgt	gac	ggg	gac	cgc	cgg	ctc	ctg	ccc	gcc	gct	gtg	cac	agc	gtg	acc	1008	
Arg	Asp	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser	Val	Thr		
				325					330					335			
cta	agc	gag	gag	gcc	gcg	ggc	gcc	tac	gcg	ccg	ctc	acg	gcc	cag	ggc	1056	
Leu	Ser	Glu	Glu	Ala	Ala	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Ala	Gln	Gly		
			340					345					350				
acc	att	ctc	atc	aac	cgg	gtg	ctg	gcc	tcg	tgc	tac	gcg	gtc	atc	gag	1104	
Thr	Ile	Leu	Ile	Asn	Arg	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Ile	Glu		
		355					360					365					
gag	cac	agc	tgg	gcg	cac	cgg	gcc	ttc	gcg	ccc	ttc	cgc	ctg	gcg	cac	1152	
Glu	His	Ser	Trp	Ala	His	Arg	Ala	Phe	Ala	Pro	Phe	Arg	Leu	Ala	His		
	370					375					380						
gcg	ctc	ctg	gct	gca	ctg	gcg	ccc	gcg	cgc	acg	gac	cgc	ggc	ggg	gac	1200	
Ala	Leu	Leu	Ala	Ala	Leu	Ala	Pro	Ala	Arg	Thr	Asp	Arg	Gly	Gly	Asp		
385					390					395					400		
agc	ggc	ggc	ggg	gac	cgc	ggg	ggc	ggc	ggc	ggc	aga	gta	gcc	cta	acc	1248	
Ser	Gly	Gly	Gly	Asp	Arg	Gly	Gly	Gly	Gly	Gly	Arg	Val	Ala	Leu	Thr		
				405					410					415			
gct	cca	ggt	gct	gcc	gac	gct	ccg	ggt	gcg	ggg	gcc	acc	gcg	ggc	atc	1296	
Ala	Pro	Gly	Ala	Ala	Asp	Ala	Pro	Gly	Ala	Gly	Ala	Thr	Ala	Gly	Ile		
			420					425					430				
cac	tgg	tac	tcg	cag	ctg	ctc	tac	caa	ata	ggc	acc	tgg	ctc	ctg	gac	1344	
His	Trp	Tyr	Ser	Gln	Leu	Leu	Tyr	Gln	Ile	Gly	Thr	Trp	Leu	Leu	Asp		
		435					440					445					
agc	gag	gcc	ctg	cac	ccg	ctg	ggc	atg	gcg	gtc	aag	tcc	agc	nnn	agc	1392	
Ser	Glu	Ala	Leu	His	Pro	Leu	Gly	Met	Ala	Val	Lys	Ser	Ser	Xaa	Ser		
	450					455					460						
cgg	ggg	gcc	ggg	gga	ggg	gcg	cgg	gag	ggg	gcc						1425	
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<211> 1622

<212> DNA

<213> human Ihh

<220>

<221> CDS

<222> (51) .. (1283)

<400> 7

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Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu Leu Leu	
5 10 15	
ctg ctg gtg gtg ccc gcg gca tgg ggc tgc ggg ccg ggt cgg gtg gtg	152
Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg Val Val	
20 25 30	
ggc agc cgc cgg cga ccg cca cgc aaa ctc gtg ccg ctc gcc tac aag	200
Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala Tyr Lys	
35 40 45 50	
cag ttc agc ccc aat gtg ccc gag aag acc ctg ggc gcc agc gga cgc	248
Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser Gly Arg	
55 60 65	
tat gaa ggc aag atc gct cgc agc tcc gag cgc ttc aag gag ctc acc	296
Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu Leu Thr	
70 75 80	
ccc aat tac aat cca gac atc atc ttc aag gac gag gag aac aca ggc	344
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly	
85 90 95	
gcc gac cgc ctc atg acc cag cgc tgc aag gac cgc ctg aac tcg ctg	392
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu	
100 105 110	
gct atc tcg gtg atg aac cag tgg ccc ggt gtg aag ctg cgg gtg acc	440
Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr	
115 120 125 130	
gag ggc tgg gac gag gac ggc cac cac tca gag gag tcc ctg cat tat	488
Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr	
135 140 145	
gag ggc cgc gcg gtg gac atc acc aca tca gac cgc gac cgc aat aag	536
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys	
150 155 160	
tat gga ctg ctg gcg cgc ttg gca gtg gag gcc ggc ttt gac tgg gtg	584
Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val	
165 170 175	
tat tac gag tca aag gcc cac gtg cat tgc tcc gtc aag tcc gag cac	632
Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu His	
180 185 190	
tcg gcc gca gcc aag acg ggc ggc tgc ttc cct gcc gga gcc cag gta	680

Ser	Ala	Ala	Ala	Lys	Thr	Gly	Gly	Cys	Phe	Pro	Ala	Gly	Ala	Gln	Val		
195					200					205					210		
cgc	ctg	gag	agt	ggg	gcg	cgt	gtg	gcc	ttg	tca	gcc	gtg	agg	ccg	gga		728
Arg	Leu	Glu	Ser	Gly	Ala	Arg	Val	Ala	Leu	Ser	Ala	Val	Arg	Pro	Gly		
				215					220					225			
gac	cgt	gtg	ctg	gcc	atg	ggg	gag	gat	ggg	agc	ccc	acc	ttc	agc	gat		776
Asp	Arg	Val	Leu	Ala	Met	Gly	Glu	Asp	Gly	Ser	Pro	Thr	Phe	Ser	Asp		
			230					235					240				
gtg	ctc	att	ttc	ctg	gac	cgc	gag	ccc	cac	agg	ctg	aga	gcc	ttc	cag		824
Val	Leu	Ile	Phe	Leu	Asp	Arg	Glu	Pro	His	Arg	Leu	Arg	Ala	Phe	Gln		
		245					250					255					
gtc	atc	gag	act	cag	gac	ccc	cca	cgc	cgc	ctg	gca	ctc	aca	ccc	gct		872
Val	Ile	Glu	Thr	Gln	Asp	Pro	Pro	Arg	Arg	Leu	Ala	Leu	Thr	Pro	Ala		
	260					265					270						
cac	ctg	ctc	ttt	acg	gct	gac	aat	cac	acg	gag	ccg	gca	gcc	cgc	ttc		920
His	Leu	Leu	Phe	Thr	Ala	Asp	Asn	His	Thr	Glu	Pro	Ala	Ala	Arg	Phe		
	275				280					285				290			
cgg	gcc	aca	ttt	gcc	agc	cac	gtg	cag	cct	ggc	cag	tac	gtg	ctg	gtg		968
Arg	Ala	Thr	Phe	Ala	Ser	His	Val	Gln	Pro	Gly	Gln	Tyr	Val	Leu	Val		
				295					300					305			
gct	ggg	gtg	cca	ggc	ctg	cag	cct	gcc	cgc	gtg	gca	gct	gtc	tct	aca		1016
Ala	Gly	Val	Pro	Gly	Leu	Gln	Pro	Ala	Arg	Val	Ala	Ala	Val	Ser	Thr		
			310					315					320				
cac	gtg	gcc	ctc	ggg	gcc	tac	gcc	ccg	ctc	aca	aag	cat	ggg	aca	ctg		1064
His	Val	Ala	Leu	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Lys	His	Gly	Thr	Leu		
		325					330					335					
gtg	gtg	gag	gat	gtg	gtg	gca	tcc	tgc	ttc	gcg	gcc	gtg	gct	gac	cac		1112
Val	Val	Glu	Asp	Val	Val	Ala	Ser	Cys	Phe	Ala	Ala	Val	Ala	Asp	His		
		340				345					350						
cac	ctg	gct	cag	ttg	gcc	ttc	tgg	ccc	ctg	aga	ctc	ttt	cac	agc	ttg		1160
His	Leu	Ala	Gln	Leu	Ala	Phe	Trp	Pro	Leu	Arg	Leu	Phe	His	Ser	Leu		
	355				360					365				370			
gca	tgg	ggc	agc	tgg	acc	ccg	ggg	gag	ggt	gtg	cat	tgg	tac	ccc	cag		1208
Ala	Trp	Gly	Ser	Trp	Thr	Pro	Gly	Glu	Gly	Val	His	Trp	Tyr	Pro	Gln		
				375					380					385			
ctg	ctc	tac	cgc	ctg	ggg	cgt	ctc	ctg	cta	gaa	gag	ggc	agc	ttc	cac		1256
Leu	Leu	Tyr	Arg	Leu	Gly	Arg	Leu	Leu	Leu	Glu	Glu	Gly	Ser	Phe	His		
			390					395					400				
cca	ctg	ggc	atg	tcc	ggg	gca	ggg	agc	tgaaaggact ccaccgctgc								1303
Pro	Leu	Gly	Met	Ser	Gly	Ala	Gly	Ser									
		405					410										
cctcctggaa ctgctgtact ggggtccagaa gcctctcagc caggagggag ctggccctgg																	1363

aagggacctg agctggggga cactggctcc tgccatctcc tctgcatga agatacacca 1423
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<220>
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 <222> (1)..(1188)

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 1 5 10 15
 gcg ctg cca gcc cag agc tgc ggg ccg ggc cgg ggg ccg gtt ggc cgg 96
 Ala Leu Pro Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
 20 25 30
 cgc cgc tat gcg cgc aag cag ctc gtg ccg cta ctc tac aag caa ttt 144
 Arg Arg Tyr Ala Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
 35 40 45
 gtg ccc ggc gtg cca gag cgg acc ctg ggc gcc agt ggg cca gcg gag 192
 Val Pro Gly Val Pro Glu Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu
 50 55 60
 ggg agg gtg gca agg ggc tcc gag cgc ttc cgg gac ctc gtg ccc aac 240
 Gly Arg Val Ala Arg Gly Ser Glu Arg Phe Arg Asp Leu Val Pro Asn
 65 70 75 80
 tac aac ccc gac atc atc ttc aag gat gag gag aac agt gga gcc gac 288
 Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp
 85 90 95
 cgc ctg atg acc gag cgt tgc aag gag agg gtg aac gct ttg gcc att 336
 Arg Leu Met Thr Glu Arg Cys Lys Glu Arg Val Asn Ala Leu Ala Ile
 100 105 110
 gcc gtg atg aac atg tgg ccc gga gtg cgc cta cga gtg act gag ggc 384
 Ala Val Met Asn Met Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly
 115 120 125
 tgg gac gag gac ggc cac cac gct cag gat tca ctc cac tac gaa ggc 432
 Trp Asp Glu Asp Gly His His Ala Gln Asp Ser Leu His Tyr Glu Gly
 130 135 140
 cgt gct ttg gac atc act acg tct gac cgc gac cgc aac aag tat ggg 480

Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly	
145					150					155					160	
ttg	ctg	gcg	cgc	ctc	gca	gtg	gaa	gcc	ggc	ttc	gac	tgg	gtc	tac	tac	528
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	
				165					170					175		
gag	tcc	cgc	aac	cac	gtc	cac	gtg	tcg	gtc	aaa	gct	gat	aac	tca	ctg	576
Glu	Ser	Arg	Asn	His	Val	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu	
			180					185					190			
gcg	gtc	cgg	gcg	ggc	ggc	tgc	ttt	ccg	gga	aat	gca	act	gtg	cgc	ctg	624
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu	
		195					200					205				
tgg	agc	ggc	gag	cgg	aaa	ggg	ctg	cgg	gaa	ctg	cac	cgc	gga	gac	tgg	672
Trp	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp	
	210					215					220					
gtt	ttg	gcg	gcc	gat	gcg	tca	ggc	cgg	gtg	gtg	ccc	acg	ccg	gtg	ctg	720
Val	Leu	Ala	Ala	Asp	Ala	Ser	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu	
225					230				235						240	
ctc	ttc	ctg	gac	cgg	gac	ttg	cag	cgc	cgg	gct	tca	ttt	gtg	gct	gtg	768
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val	
				245				250					255			
gag	acc	gag	tgg	cct	cca	cgc	aaa	ctg	ttg	ctc	acg	ccc	tgg	cac	ctg	816
Glu	Thr	Glu	Trp	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu	
			260					265					270			
gtg	ttt	gcc	gct	cga	ggg	ccg	gcg	ccc	gcg	cca	ggc	gac	ttt	gca	ccg	864
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro	
		275					280				285					
gtg	ttc	gcg	cgc	cgg	cta	cgc	gct	ggg	gac	tcg	gtg	ctg	gcg	ccc	ggc	912
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly	
	290					295					300					
ggg	gat	gcg	ctt	cgg	cca	gcg	cgc	gtg	gcc	cgt	gtg	gcg	cgg	gag	gaa	960
Gly	Asp	Ala	Leu	Arg	Pro	Ala	Arg	Val	Ala	Arg	Val	Ala	Arg	Glu	Glu	
305					310					315					320	
gcc	gtg	ggc	gtg	ttc	gcg	ccg	ctc	acc	gcg	cac	ggg	acg	ctg	ctg	gtg	1008
Ala	Val	Gly	Val	Phe	Ala	Pro	Leu	Thr	Ala	His	Gly	Thr	Leu	Leu	Val	
				325					330				335			
aac	gat	gtc	ctg	gcc	tct	tgc	tac	gcg	gtt	ctg	gag	agt	cac	cag	tgg	1056
Asn	Asp	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Leu	Glu	Ser	His	Gln	Trp	
			340					345					350			
gcg	cac	cgc	gct	ttt	gcc	ccc	ttg	aga	ctg	ctg	cac	gcg	cta	ggg	gcg	1104
Ala	His	Arg	Ala	Phe	Ala	Pro	Leu	Arg	Leu	Leu	His	Ala	Leu	Gly	Ala	
		355					360				365					
ctg	ctc	ccc	ggc	ggg	gcc	gtc	cag	ccg	act	ggc	atg	cat	tgg	tac	tct	1152
Leu	Leu	Pro	Gly	Gly	Ala	Val	Gln	Pro	Thr	Gly	Met	His	Trp	Tyr	Ser	

370	375	380	
cgg ctc ctc tac cgc tta gcg gag gag cta ctg ggc tg Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly 385 390 395			1190
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agc ttg ctt ctg acg cct tgt gga tta gcc tgt ggt cct ggt aga ggt Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly 20 25 30			96
tat gga aaa cga aga cac cca aag aaa tta acc ccg ttg gct tac aag Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys 35 40 45			144
caa ttc atc ccc aac gtt gct gag aaa acg ctt gga gcc agc ggc aaa Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys 50 55 60			192
tac gaa ggc aaa atc aca agg aat tca gag aga ttt aaa gag ctg att Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile 65 70 75 80			240
ccg aat tat aat ccc gat atc atc ttt aag gac gag gaa aac aca aac Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn 85 90 95			288
gct gac agg ctg atg acc aag cgc tgt aag gac aag tta aat tcg ttg Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu 100 105 110			336
gcc ata tcc gtc atg aac cac tgg ccc ggc gtg aaa ctg cgc gtc act Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr 115 120 125			384
gaa ggc tgg gat gag gat ggt cac cat tta gaa gaa tct ttg cac tat Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr 130 135 140			432
gag gga cgg gca gtg gac atc act acc tca gac agg gat aaa agc aag Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys 145 150 155 160			480
tat ggg atg cta tcc agg ctt gca gtg gag gca gga ttc gac tgg gtc 			528

Tyr	Gly	Met	Leu	Ser	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val		
				165					170					175			
tat	tat	gaa	tct	aaa	gcc	cac	ata	cac	tgc	tct	gtc	aaa	gca	gaa	aat	576	
Tyr	Tyr	Glu	Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn		
			180					185					190				
tca	gtg	gct	gct	aaa	tca	gga	gga	tgt	ttt	cct	ggg	tct	ggg	acg	gtg	624	
Ser	Val	Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Gly	Thr	Val		
		195					200					205					
aca	ctt	ggg	gat	ggg	acg	agg	aaa	ccc	atc	aaa	gat	ctt	aaa	gtg	ggc	672	
Thr	Leu	Gly	Asp	Gly	Thr	Arg	Lys	Pro	Ile	Lys	Asp	Leu	Lys	Val	Gly		
	210					215					220						
gac	cgg	gtt	ttg	gct	gca	gac	gag	aag	gga	aat	gtc	tta	ata	agc	gac	720	
Asp	Arg	Val	Leu	Ala	Ala	Asp	Glu	Lys	Gly	Asn	Val	Leu	Ile	Ser	Asp		
	225				230					235					240		
ttt	att	atg	ttt	ata	gac	cac	gat	ccg	aca	acg	aga	agg	caa	ttc	atc	768	
Phe	Ile	Met	Phe	Ile	Asp	His	Asp	Pro	Thr	Thr	Arg	Arg	Gln	Phe	Ile		
				245				250						255			
gtc	atc	gag	acg	tca	gaa	cct	ttc	acc	aag	ctc	acc	ctc	act	gcc	gcg	816	
Val	Ile	Glu	Thr	Ser	Glu	Pro	Phe	Thr	Lys	Leu	Thr	Leu	Thr	Ala	Ala		
			260					265					270				
cac	cta	gtt	ttc	gtt	gga	aac	tct	tca	gca	gct	tcg	ggg	ata	aca	gca	864	
His	Leu	Val	Phe	Val	Gly	Asn	Ser	Ser	Ala	Ala	Ser	Gly	Ile	Thr	Ala		
		275					280					285					
aca	ttt	gcc	agc	aac	gtg	aag	cct	gga	gat	aca	gtt	tta	gtg	tgg	gaa	912	
Thr	Phe	Ala	Ser	Asn	Val	Lys	Pro	Gly	Asp	Thr	Val	Leu	Val	Trp	Glu		
	290					295					300						
gac	aca	tgc	gag	agc	ctc	aag	agc	gtt	aca	gtg	aaa	agg	att	tac	act	960	
Asp	Thr	Cys	Glu	Ser	Leu	Lys	Ser	Val	Thr	Val	Lys	Arg	Ile	Tyr	Thr		
	305				310					315					320		
gag	gag	cac	gag	ggc	tct	ttt	gcg	cca	gtc	acc	gcg	cac	gga	acc	ata	1008	
Glu	Glu	His	Glu	Gly	Ser	Phe	Ala	Pro	Val	Thr	Ala	His	Gly	Thr	Ile		
				325				330						335			
ata	gtg	gat	cag	gtg	ttg	gca	tcg	tgc	tac	gcg	gtc	att	gag	aac	cac	1056	
Ile	Val	Asp	Gln	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Ile	Glu	Asn	His		
			340					345					350				
aaa	tgg	gca	cat	tgg	gct	ttt	gcg	ccg	gtc	agg	ttg	tgt	cac	aag	ctg	1104	
Lys	Trp	Ala	His	Trp	Ala	Phe	Ala	Pro	Val	Arg	Leu	Cys	His	Lys	Leu		
		355					360					365					
atg	acg	tgg	ctt	ttt	ccg	gct	cgt	gaa	tca	aac	gtc	aat	ttt	cag	gag	1152	
Met	Thr	Trp	Leu	Phe	Pro	Ala	Arg	Glu	Ser	Asn	Val	Asn	Phe	Gln	Glu		
		370				375					380						
gat	ggg	atc	cac	tgg	tac	tca	aat	atg	ctg	ttt	cac	atc	ggc	tct	tgg	1200	
Asp	Gly	Ile	His	Trp	Tyr	Ser	Asn	Met	Leu	Phe	His	Ile	Gly	Ser	Trp		

385		390		395		400	
ctg ctg gac aga gac tct ttc cat cca ctc ggg att tta cac tta agt							1248
Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser							
	405			410		415	
tga							1251
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Cys Ala Leu Leu Val Ser Ser Gly Leu Thr Cys Gly Pro Gly Arg Gly							
	20			25		30	
Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys							
	35			40		45	
Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg							
	50			55		60	
Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr							
	65			70		75	80
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly							
		85			90		95
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu							
	100			105		110	
Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr							
	115			120		125	
Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr							
	130			135		140	
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys							
	145			150		155	160
Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val							
		165			170		175
Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn							
	180				185		190
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val							
	195			200		205	
His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly							
	210			215		220	
Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp							

225		230		235		240									
Phe	Leu	Thr	Phe	Leu	Asp	Arg	Met	Asp	Ser	Ser	Arg	Lys	Leu	Phe	Tyr
				245					250					255	
Val	Ile	Glu	Thr	Arg	Gln	Pro	Arg	Ala	Arg	Leu	Leu	Leu	Thr	Ala	Ala
			260					265					270		
His	Leu	Leu	Phe	Val	Ala	Pro	Gln	His	Asn	Gln	Ser	Glu	Ala	Thr	Gly
		275					280					285			
Ser	Thr	Ser	Gly	Gln	Ala	Leu	Phe	Ala	Ser	Asn	Val	Lys	Pro	Gly	Gln
	290					295					300				
Arg	Val	Tyr	Val	Leu	Gly	Glu	Gly	Gly	Gln	Gln	Leu	Leu	Pro	Ala	Ser
305					310					315					320
Val	His	Ser	Val	Ser	Leu	Arg	Glu	Glu	Ala	Ser	Gly	Ala	Tyr	Ala	Pro
				325					330					335	
Leu	Thr	Ala	Gln	Gly	Thr	Ile	Leu	Ile	Asn	Arg	Val	Leu	Ala	Ser	Cys
			340					345					350		
Tyr	Ala	Val	Ile	Glu	Glu	His	Ser	Trp	Ala	His	Trp	Ala	Phe	Ala	Pro
		355					360					365			
Phe	Arg	Leu	Ala	Gln	Gly	Leu	Leu	Ala	Ala	Leu	Cys	Pro	Asp	Gly	Ala
	370					375					380				
Ile	Pro	Thr	Ala	Ala	Thr	Thr	Thr	Thr	Gly	Ile	His	Trp	Tyr	Ser	Arg
385					390					395					400
Leu	Leu	Tyr	Arg	Ile	Gly	Ser	Trp	Val	Leu	Asp	Gly	Asp	Ala	Leu	His
				405					410					415	
Pro	Leu	Gly	Met	Val	Ala	Pro	Ala	Ser							
			420					425							

<210> 11
 <211> 396
 <212> PRT
 <213> mouse Dhh

<400> 11															
Met	Ala	Leu	Pro	Ala	Ser	Leu	Leu	Pro	Leu	Cys	Cys	Leu	Ala	Leu	Leu
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Ala	Leu	Ser	Ala	Gln	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Pro	Val	Gly	Arg
			20					25					30		
Arg	Arg	Tyr	Val	Arg	Lys	Gln	Leu	Val	Pro	Leu	Leu	Tyr	Lys	Gln	Phe
		35					40					45			
Val	Pro	Ser	Met	Pro	Glu	Arg	Thr	Leu	Gly	Ala	Ser	Gly	Pro	Ala	Glu
	50					55					60				
Gly	Arg	Val	Thr	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn

65				70				75				80			
Tyr	Asn	Pro	Asp	Ile 85	Ile	Phe	Lys	Asp	Glu 90	Glu	Asn	Ser	Gly	Ala 95	Asp
Arg	Leu	Met	Thr 100	Glu	Arg	Cys	Lys	Glu 105	Arg	Val	Asn	Ala	Leu 110	Ala	Ile
Ala	Val	Met 115	Asn	Met	Trp	Pro	Gly 120	Val	Arg	Leu	Arg	Val 125	Thr	Glu	Gly
Trp	Asp 130	Glu	Asp	Gly	His	His 135	Ala	Gln	Asp	Ser	Leu 140	His	Tyr	Glu	Gly
Arg 145	Ala	Leu	Asp	Ile	Thr 150	Thr	Ser	Asp	Arg	Asp 155	Arg	Asn	Lys	Tyr	Gly 160
Leu	Leu	Ala	Arg	Leu 165	Ala	Val	Glu	Ala	Gly 170	Phe	Asp	Trp	Val	Tyr 175	Tyr
Glu	Ser	Arg	Asn 180	His	Ile	His	Val	Ser 185	Val	Lys	Ala	Asp	Asn 190	Ser	Leu
Ala	Val	Arg 195	Ala	Gly	Gly	Cys	Phe 200	Pro	Gly	Asn	Ala	Thr 205	Val	Arg	Leu
Arg	Ser 210	Gly	Glu	Arg	Lys	Gly 215	Leu	Arg	Glu	Leu	His 220	Arg	Gly	Asp	Trp
Val 225	Leu	Ala	Ala	Asp	Ala 230	Ala	Gly	Arg	Val	Val 235	Pro	Thr	Pro	Val	Leu 240
Leu	Phe	Leu	Asp	Arg 245	Asp	Leu	Gln	Arg	Arg 250	Ala	Ser	Phe	Val	Ala 255	Val
Glu	Thr	Glu	Arg 260	Pro	Pro	Arg	Lys	Leu 265	Leu	Leu	Thr	Pro	Trp 270	His	Leu
Val	Phe 275	Ala	Ala	Arg	Gly	Pro	Ala 280	Pro	Ala	Pro	Gly	Asp 285	Phe	Ala	Pro
Val 290	Phe	Ala	Arg	Arg	Leu	Arg 295	Ala	Gly	Asp	Ser	Val 300	Leu	Ala	Pro	Gly
Gly 305	Asp	Ala	Leu	Gln	Pro 310	Ala	Arg	Val	Ala	Arg 315	Val	Ala	Arg	Glu	Glu 320
Ala	Val	Gly	Val	Phe 325	Ala	Pro	Leu	Thr	Ala 330	His	Gly	Thr	Leu	Leu 335	Val
Asn	Asp	Val	Leu 340	Ala	Ser	Cys	Tyr	Ala 345	Val	Leu	Glu	Ser	His 350	Gln	Trp
Ala	His 355	Arg	Ala	Phe	Ala	Pro	Leu 360	Arg	Leu	Leu	His 365	Ala	Leu	Gly	Ala
Leu	Leu	Pro	Gly	Gly	Ala	Val	Gln	Pro	Thr	Gly	Met	His	Trp	Tyr	Ser

370 375 380
 Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly
 385 390 395

 <210> 12
 <211> 411
 <212> PRT
 <213> mouse Ihh

 <400> 12
 Met Ser Pro Ala Trp Leu Arg Pro Arg Leu Arg Phe Cys Leu Phe Leu
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 Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
 20 25 30

 Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
 35 40 45

 Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
 50 55 60

 Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65 70 75 80

 Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
 85 90 95

 Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
 100 105 110

 Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
 115 120 125

 Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
 130 135 140

 His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
 145 150 155 160

 Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
 165 170 175

 Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
 180 185 190

 Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
 195 200 205

 Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
 210 215 220

 Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
 225 230 235 240

 Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala

100							105					110						
Ser	Val	Met	Asn	Gln	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly			
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Trp	Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly			
	130					135					140							
Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Ser	Lys	Tyr	Gly			
145					150					155					160			
Met	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr			
				165					170					175				
Glu	Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val			
			180					185					190					
Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Ala	Thr	Val	His	Leu			
		195					200					205						
Glu	Gln	Gly	Gly	Thr	Lys	Leu	Val	Lys	Asp	Leu	Arg	Pro	Gly	Asp	Arg			
	210					215					220							
Val	Leu	Ala	Ala	Asp	Asp	Gln	Gly	Arg	Leu	Leu	Tyr	Ser	Asp	Phe	Leu			
225					230					235					240			
Thr	Phe	Leu	Asp	Arg	Asp	Glu	Gly	Ala	Lys	Lys	Val	Phe	Tyr	Val	Ile			
				245					250					255				
Glu	Thr	Leu	Glu	Pro	Arg	Glu	Arg	Leu	Leu	Leu	Thr	Ala	Ala	His	Leu			
			260					265					270					
Leu	Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Gly	Pro	Thr	Pro	Gly	Pro	Ser			
		275					280					285						
Ala	Leu	Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val			
	290					295					300							
Ala	Glu	Arg	Gly	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser			
305					310					315					320			
Val	Thr	Leu	Arg	Glu	Glu	Glu	Ala	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Ala			
				325					330					335				
His	Gly	Thr	Ile	Leu	Ile	Asn	Arg	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val			
			340					345					350					
Ile	Glu	Glu	His	Ser	Trp	Ala	His	Arg	Ala	Phe	Ala	Pro	Phe	Arg	Leu			
		355					360					365						
Ala	His	Ala	Leu	Leu	Ala	Ala	Leu	Ala	Pro	Ala	Arg	Thr	Asp	Gly	Gly			
	370					375					380							
Gly	Gly	Gly	Ser	Ile	Pro	Ala	Ala	Gln	Ser	Ala	Thr	Glu	Ala	Arg	Gly			
385					390					395					400			
Ala	Glu	Pro	Thr	Ala	Gly	Ile	His	Trp	Tyr	Ser	Gln	Leu	Leu	Tyr	His			

405 410 415
 Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
 420 425 430
 Ala Val Lys Ser Ser
 435
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 <212> PRT
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 Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
 35 40 45
 Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
 50 55 60
 Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
 65 70 75 80
 Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
 85 90 95
 Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
 100 105 110
 Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
 115 120 125
 Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
 130 135 140
 Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
 145 150 155 160
 Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
 165 170 175
 Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
 180 185 190
 Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
 195 200 205
 Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
 210 215 220
 Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met

225					230						235				240
Phe	Thr	Asp	Arg	Asp	Ser	Thr	Thr	Arg	Arg	Val	Phe	Tyr	Val	Ile	Glu
				245					250					255	
Thr	Gln	Glu	Pro	Val	Glu	Lys	Ile	Thr	Leu	Thr	Ala	Ala	His	Leu	Leu
			260					265					270		
Phe	Val	Leu	Asp	Asn	Ser	Thr	Glu	Asp	Leu	His	Thr	Met	Thr	Ala	Ala
		275					280					285			
Tyr	Ala	Ser	Ser	Val	Arg	Ala	Gly	Gln	Lys	Val	Met	Val	Val	Asp	Asp
	290					295					300				
Ser	Gly	Gln	Leu	Lys	Ser	Val	Ile	Val	Gln	Arg	Ile	Tyr	Thr	Glu	Glu
305					310					315					320
Gln	Arg	Gly	Ser	Phe	Ala	Pro	Val	Thr	Ala	His	Gly	Thr	Ile	Val	Val
				325					330					335	
Asp	Arg	Ile	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Ile	Glu	Asp	Gln	Gly	Leu
			340					345					350		
Ala	His	Leu	Ala	Phe	Ala	Pro	Ala	Arg	Leu	Tyr	Tyr	Tyr	Val	Ser	Ser
		355					360					365			
Phe	Leu	Ser	Pro	Lys	Thr	Pro	Ala	Val	Gly	Pro	Met	Arg	Leu	Tyr	Asn
	370					375					380				
Arg	Arg	Gly	Ser	Thr	Gly	Thr	Pro	Gly	Ser	Cys	His	Gln	Met	Gly	Thr
385					390					395					400
Trp	Leu	Leu	Asp	Ser	Asn	Met	Leu	His	Pro	Leu	Gly	Met	Ser	Val	Asn
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Ser Ser

<210> 15

<211> 475

<212> PRT

<213> human Shh

<220>

<223> Xaa at position 463 is any or unknown amino acid

<400> 15

Met	Leu	Leu	Leu	Ala	Arg	Cys	Leu	Leu	Leu	Val	Leu	Val	Ser	Ser	Leu
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Leu	Val	Cys	Ser	Gly	Leu	Ala	Cys	Gly	Pro	Gly	Arg	Gly	Phe	Gly	Lys
			20					25					30		

Arg	Arg	His	Pro	Lys	Lys	Leu	Thr	Pro	Leu	Ala	Tyr	Lys	Gln	Phe	Ile
		35					40					45			

Pro	Asn	Val	Ala	Glu	Lys	Thr	Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly
	50					55					60				

Lys	Ile	Ser	Arg	Asn	Ser	Glu	Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr		
65					70					75					80		
Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg		
			85						90					95			
Leu	Met	Thr	Gln	Arg	Cys	Lys	Asp	Lys	Leu	Asn	Ala	Leu	Ala	Ile	Ser		
			100					105					110				
Val	Met	Asn	Gln	Trp	Pro	Gly	Val	Lys	Leu	Arg	Val	Thr	Glu	Gly	Trp		
		115					120					125					
Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg		
	130					135					140						
Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Ser	Lys	Tyr	Gly	Met		
145					150					155					160		
Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu		
			165					170						175			
Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala		
		180						185					190				
Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Ala	Thr	Val	His	Leu	Glu		
		195					200					205					
Gln	Gly	Gly	Thr	Lys	Leu	Val	Lys	Asp	Leu	Ser	Pro	Gly	Asp	Arg	Val		
	210					215					220						
Leu	Ala	Ala	Asp	Asp	Gln	Gly	Arg	Leu	Leu	Tyr	Ser	Asp	Phe	Leu	Thr		
225					230					235					240		
Phe	Leu	Asp	Arg	Asp	Asp	Gly	Ala	Lys	Lys	Val	Phe	Tyr	Val	Ile	Glu		
			245						250					255			
Thr	Arg	Glu	Pro	Arg	Glu	Arg	Leu	Leu	Leu	Thr	Ala	Ala	His	Leu	Leu		
		260						265					270				
Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Ala	Thr	Gly	Glu	Pro	Glu	Ala	Ser		
		275					280					285					
Ser	Gly	Ser	Gly	Pro	Pro	Ser	Gly	Gly	Ala	Leu	Gly	Pro	Arg	Ala	Leu		
	290					295					300						
Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val	Ala	Glu		
305					310					315					320		
Arg	Asp	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser	Val	Thr		
			325						330					335			
Leu	Ser	Glu	Glu	Ala	Ala	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Ala	Gln	Gly		
		340					345						350				
Thr	Ile	Leu	Ile	Asn	Arg	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Ile	Glu		
		355					360					365					

Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
370 375 380

Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
385 390 395 400

Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
405 410 415

Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
420 425 430

His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
435 440 445

Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser
450 455 460

Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
465 470 475

<210> 16

<211> 411

<212> PRT

<213> human Ihh

<400> 16

Met Ser Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu
1 5 10 15

Leu Leu Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg
20 25 30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
35 40 45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
50 55 60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
65 70 75 80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
85 90 95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
100 105 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
115 120 125

Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
130 135 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
145 150 155 160

Asn	Lys	Tyr	Gly	Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	165	170	175
Trp	Val	Tyr	Tyr	Glu	Ser	Lys	Ala	His	Val	His	Cys	Ser	Val	Lys	Ser	180	185	190
Glu	His	Ser	Ala	Ala	Ala	Lys	Thr	Gly	Gly	Cys	Phe	Pro	Ala	Gly	Ala	195	200	205
Gln	Val	Arg	Leu	Glu	Ser	Gly	Ala	Arg	Val	Ala	Leu	Ser	Ala	Val	Arg	210	215	220
Pro	Gly	Asp	Arg	Val	Leu	Ala	Met	Gly	Glu	Asp	Gly	Ser	Pro	Thr	Phe	225	230	235
Ser	Asp	Val	Leu	Ile	Phe	Leu	Asp	Arg	Glu	Pro	His	Arg	Leu	Arg	Ala	245	250	255
Phe	Gln	Val	Ile	Glu	Thr	Gln	Asp	Pro	Pro	Arg	Arg	Leu	Ala	Leu	Thr	260	265	270
Pro	Ala	His	Leu	Leu	Phe	Thr	Ala	Asp	Asn	His	Thr	Glu	Pro	Ala	Ala	275	280	285
Arg	Phe	Arg	Ala	Thr	Phe	Ala	Ser	His	Val	Gln	Pro	Gly	Gln	Tyr	Val	290	295	300
Leu	Val	Ala	Gly	Val	Pro	Gly	Leu	Gln	Pro	Ala	Arg	Val	Ala	Ala	Val	305	310	315
Ser	Thr	His	Val	Ala	Leu	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Lys	His	Gly	325	330	335
Thr	Leu	Val	Val	Glu	Asp	Val	Val	Ala	Ser	Cys	Phe	Ala	Ala	Val	Ala	340	345	350
Asp	His	His	Leu	Ala	Gln	Leu	Ala	Phe	Trp	Pro	Leu	Arg	Leu	Phe	His	355	360	365
Ser	Leu	Ala	Trp	Gly	Ser	Trp	Thr	Pro	Gly	Glu	Gly	Val	His	Trp	Tyr	370	375	380
Pro	Gln	Leu	Leu	Tyr	Arg	Leu	Gly	Arg	Leu	Leu	Leu	Glu	Glu	Gly	Ser	385	390	395
Phe	His	Pro	Leu	Gly	Met	Ser	Gly	Ala	Gly	Ser						405	410	

<210> 17

<211> 396

<212> PRT

<213> human Dhh

<400> 17

Met	Ala	Leu	Leu	Thr	Asn	Leu	Leu	Pro	Leu	Cys	Cys	Leu	Ala	Leu	Leu	1	5	10	15
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	---	---	----	----

Ala	Leu	Pro	Ala	Gln	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Pro	Val	Gly	Arg		
			20					25					30				
Arg	Arg	Tyr	Ala	Arg	Lys	Gln	Leu	Val	Pro	Leu	Leu	Tyr	Lys	Gln	Phe		
		35					40					45					
Val	Pro	Gly	Val	Pro	Glu	Arg	Thr	Leu	Gly	Ala	Ser	Gly	Pro	Ala	Glu		
	50					55					60						
Gly	Arg	Val	Ala	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn		
65					70				75						80		
Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Ser	Gly	Ala	Asp		
				85					90					95			
Arg	Leu	Met	Thr	Glu	Arg	Cys	Lys	Glu	Arg	Val	Asn	Ala	Leu	Ala	Ile		
			100					105					110				
Ala	Val	Met	Asn	Met	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly		
		115					120					125					
Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly		
	130					135					140						
Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly		
145					150					155					160		
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr		
				165					170					175			
Glu	Ser	Arg	Asn	His	Val	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu		
			180					185					190				
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu		
		195					200					205					
Trp	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp		
	210					215					220						
Val	Leu	Ala	Ala	Asp	Ala	Ser	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu		
225					230					235					240		
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val		
				245					250					255			
Glu	Thr	Glu	Trp	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu		
			260					265					270				
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro		
		275					280					285					
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly		
	290					295					300						
Gly	Asp	Ala	Leu	Arg	Pro	Ala	Arg	Val	Ala	Arg	Val	Ala	Arg	Glu	Glu		
305					310					315					320		

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
325 330 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
340 345 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
385 390 395

<210> 18

<211> 416

<212> PRT

<213> Zebrafish Thh

<400> 18

Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
1 5 10 15

Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
20 25 30

Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
85 90 95

Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
100 105 110

Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
145 150 155 160

Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
180 185 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val
 195 200 205
 Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly
 210 215 220
 Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp
 225 230 235 240
 Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile
 245 250 255
 Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala
 260 265 270
 His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala
 275 280 285
 Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu
 290 295 300
 Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr
 305 310 315 320
 Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile
 325 330 335
 Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His
 340 345 350
 Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu
 355 360 365
 Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
 370 375 380
 Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
 385 390 395 400
 Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
 405 410 415

<210> 19
 <211> 1416
 <212> DNA
 <213> Drosophila HH

<220>
 <221> CDS
 <222> (1) .. (1413)

<400> 19
 atg gat aac cac agc tca gtg cct tgg gcc agt gcc gcc agt gtc acc 48
 Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
 1 5 10 15

tgt ctc tcc ctg gga tgc caa atg cca cag ttc cag ttc cag ttc cag	96
Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln	
20 25 30	
ctc caa atc cgc agc gag ctc cat ctc cgc aag ccc gca aga aga acg	144
Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr	
35 40 45	
caa acg atg cgc cac att gcg cat acg cag cgt tgc ctc agc agg ctg	192
Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu	
50 55 60	
acc tct ctg gtg gcc ctg ctg ctg atc gtc ttg ccg atg gtc ttt agc	240
Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser	
65 70 75 80	
ccg gct cac agc tgc ggt cct ggc cga gga ttg ggt cgt cat agg gcg	288
Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala	
85 90 95	
cgc aac ctg tat ccg ctg gtc ctc aag cag aca att ccc aat cta tcc	336
Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser	
100 105 110	
gag tac acg aac agc gcc tcc gga cct ctg gag ggt gtg atc cgt cgg	384
Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg	
115 120 125	
gat tcg ccc aaa ttc aag gac ctc gtg ccc aac tac aac agg gac atc	432
Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile	
130 135 140	
ctt ttc cgt gac gag gaa ggc acc gga gcg gat ggc ttg atg agc aag	480
Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys	
145 150 155 160	
cgc tgc aag gag aag cta aac gtg ctg gcc tac tcg gtg atg aac gaa	528
Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu	
165 170 175	
tgg ccc ggc atc cgg ctg ctg gtc acc gag agc tgg gac gag gac tac	576
Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr	
180 185 190	
cat cac ggc cag gag tcg ctc cac tac gag ggc cga gcg gtg acc att	624
His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile	
195 200 205	
gcc acc tcc gat cgc gac cag tcc aaa tac ggc atg ctc gct cgc ctg	672
Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu	
210 215 220	
gcc gtc gag gct gga ttc gat tgg gtc tcc tac gtc agc agg cgc cac	720
Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His	
225 230 235 240	

atc tac tgc tcc gtc aag tca gat tcg tcg atc agt tcc cac gtg cac	768
Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His	
245 250 255	
ggc tgc ttc acg ccg gag agc aca gcg ctg ctg gag agt gga gtc cgg	816
Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg	
260 265 270	
aag ccg ctc ggc gag ctc tct atc gga gat cgt gtt ttg agc atg acc	864
Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr	
275 280 285	
gcc aac gga cag gcc gtc tac agc gaa gtg atc ctc ttc atg gac cgc	912
Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg	
290 295 300	
aac ctc gag cag atg caa aac ttt gtg cag ctg cac acg gac ggt gga	960
Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly	
305 310 315 320	
gca gtg ctc acg gtg acg ccg gct cac ctg gtt agc gtt tgg cag ccg	1008
Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro	
325 330 335	
gag agc cag aag ctc acg ttt gtg ttt gcg cat cgc atc gag gag aag	1056
Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys	
340 345 350	
aac cag gtg ctc gta cgg gat gtg gag acg ggc gag ctg agg ccc cag	1104
Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln	
355 360 365	
cga gtg gtc aag ttg ggc agt gtg cgc agt aag ggc gtg gtc gcg ccg	1152
Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro	
370 375 380	
ctg acc cgc gag ggc acc att gtg gtc aac tcg gtg gcc gcc agt tgc	1200
Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys	
385 390 395 400	
tat gcg gtg atc aac agt cag tcg ctg gcc cac tgg gga ctg gct ccc	1248
Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro	
405 410 415	
atg cgc ctg ctg tcc acg ctg gag gcg tgg ctg ccc gcc aag gag cag	1296
Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln	
420 425 430	
ttg cac agt tcg ccg aag gtg gtg agc tcg gcg cag cag cag aat ggc	1344
Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly	
435 440 445	
atc cat tgg tat gcc aat gcg ctc tac aag gtc aag gac tac gtg ctg	1392
Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu	
450 455 460	
ccg cag agc tgg cgc cac gat tga	1416

Pro Gln Ser Trp Arg His Asp
465 470

<210> 20

<211> 471

<212> PRT

<213> Drosophila HH

<400> 20

Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
1 5 10 15

Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln
20 25 30

Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr
35 40 45

Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu
50 55 60

Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser
65 70 75 80

Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala
85 90 95

Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser
100 105 110

Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg
115 120 125

Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile
130 135 140

Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys
145 150 155 160

Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
165 170 175

Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
180 185 190

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
195 200 205

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
210 215 220

Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
225 230 235 240

Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
245 250 255

Gly	Cys	Phe	Thr	Pro	Glu	Ser	Thr	Ala	Leu	Leu	Glu	Ser	Gly	Val	Arg	260	265	270
Lys	Pro	Leu	Gly	Glu	Leu	Ser	Ile	Gly	Asp	Arg	Val	Leu	Ser	Met	Thr	275	280	285
Ala	Asn	Gly	Gln	Ala	Val	Tyr	Ser	Glu	Val	Ile	Leu	Phe	Met	Asp	Arg	290	295	300
Asn	Leu	Glu	Gln	Met	Gln	Asn	Phe	Val	Gln	Leu	His	Thr	Asp	Gly	Gly	305	310	315
Ala	Val	Leu	Thr	Val	Thr	Pro	Ala	His	Leu	Val	Ser	Val	Trp	Gln	Pro	325	330	335
Glu	Ser	Gln	Lys	Leu	Thr	Phe	Val	Phe	Ala	His	Arg	Ile	Glu	Glu	Lys	340	345	350
Asn	Gln	Val	Leu	Val	Arg	Asp	Val	Glu	Thr	Gly	Glu	Leu	Arg	Pro	Gln	355	360	365
Arg	Val	Val	Lys	Leu	Gly	Ser	Val	Arg	Ser	Lys	Gly	Val	Val	Ala	Pro	370	375	380
Leu	Thr	Arg	Glu	Gly	Thr	Ile	Val	Val	Asn	Ser	Val	Ala	Ala	Ser	Cys	385	390	395
Tyr	Ala	Val	Ile	Asn	Ser	Gln	Ser	Leu	Ala	His	Trp	Gly	Leu	Ala	Pro	405	410	415
Met	Arg	Leu	Leu	Ser	Thr	Leu	Glu	Ala	Trp	Leu	Pro	Ala	Lys	Glu	Gln	420	425	430
Leu	His	Ser	Ser	Pro	Lys	Val	Val	Ser	Ser	Ala	Gln	Gln	Gln	Asn	Gly	435	440	445
Ile	His	Trp	Tyr	Ala	Asn	Ala	Leu	Tyr	Lys	Val	Lys	Asp	Tyr	Val	Leu	450	455	460
Pro	Gln	Ser	Trp	Arg	His	Asp										465	470	

<210> 21

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: degenerate
polypeptide sequence

<220>

<221> SITE

<222> 7

<223> Xaa represents Gly, Ala, Val, Leu, Ile, Phe, Tyr or Trp

<220>
<221> SITE
<222> 9
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 44
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
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<222> 85
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
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<222> 93
<223> Xaa represents Lys, Arg, His, Asn or Gln

<220>
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<222> 98
<223> Xaa represents Lys, Arg or His

<220>
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<222> 112
<223> Xaa represents Ser, Thr, Tyr, Trp or Phe

<220>
<221> SITE
<222> 132
<223> Xaa represents Lys, Arg or His

<220>
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<222> 137
<223> Xaa represents Met, Cys, Ser or Thr

<220>
<221> SITE
<222> 139
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> SITE
<222> 181
<223> Xaa represents Leu, Val, Met, Thr or Ser

<220>
<221> SITE
<222> 183
<223> Xaa represents His, Phe, Tyr, Ser, Thr, Met or Cys

<220>

<221> SITE
<222> 185
<223> Xaa represents Gln, Asn, Glu, or Asp

<220>
<221> SITE
<222> 186
<223> Xaa represents His, Phe, Tyr, Thr, Gln, Asn, Glu or Asp

<220>
<221> SITE
<222> 189
<223> Xaa represents Gln, Asn, Glu, Asp, Thr, Ser, Met or Cys

<220>
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<222> 191
<223> Xaa represents Ala, Gly, Cys, Leu, Val or Met

<220>
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<222> 196
<223> Xaa represents Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser, Thr
or Cys

<220>
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<222> 200
<223> Xaa represents Arg, Lys, Met or Ile

<220>
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<222> 206
<223> Xaa represents Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr or Met

<220>
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<223> Xaa represents Ala, Gly, Cys, Asp, Asn, Glu or Gln

<220>
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<222> 209
<223> Xaa represents Arg, Lys, Met, Ile, Asn, Asp, Glu or Gln

<220>
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<222> 211
<223> Xaa represents Leu, Val, Met or Ile

<220>
<221> SITE
<222> 212
<223> Xaa represents Phe, Tyr, Thr, His or Trp

<220>
<221> SITE

<222> 216
<223> Xaa represents Ile, Val, Leu or Met

<220>
<221> SITE
<222> 217
<223> Xaa represents Met, Cys, Ile, Leu, Val, Thr or Ser

<220>
<221> SITE
<222> 219
<223> Xaa represents Leu, Val, Met, Thr or Ser. In an even more expansive library, each Xaa can be selected from any amino acid.

<400> 21

Cys	Gly	Pro	Gly	Arg	Gly	Xaa	Gly	Xaa	Arg	Arg	His	Pro	Lys	Lys	Leu
1				5					10					15	

Thr	Pro	Leu	Ala	Tyr	Lys	Gln	Phe	Ile	Pro	Asn	Val	Ala	Glu	Lys	Thr
			20					25					30		

Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly	Lys	Ile	Xaa	Arg	Asn	Ser	Glu
		35					40					45			

Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys
	50					55					60				

Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	Leu	Met	Thr	Gln	Arg	Cys	Lys
65					70					75					80

Asp	Lys	Leu	Asn	Xaa	Leu	Ala	Ile	Ser	Val	Met	Asn	Xaa	Trp	Pro	Gly
			85						90					95	

Val	Xaa	Leu	Arg	Val	Thr	Glu	Gly	Trp	Asp	Glu	Asp	Gly	His	His	Xaa
			100					105					110		

Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser
		115					120					125			

Asp	Arg	Asp	Xaa	Ser	Lys	Tyr	Gly	Xaa	Leu	Xaa	Arg	Leu	Ala	Val	Glu
	130					135					140				

Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu	Ser	Lys	Ala	His	Ile	His	Cys
145					150					155					160

Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe
				165					170					175	

Pro	Gly	Ser	Ala	Xaa	Val	Xaa	Leu	Xaa	Xaa	Gly	Gly	Xaa	Lys	Xaa	Val
			180					185					190		

Lys	Asp	Leu	Xaa	Pro	Gly	Asp	Xaa	Val	Leu	Ala	Ala	Asp	Xaa	Xaa	Gly
		195					200					205			

Xaa	Leu	Xaa	Xaa	Ser	Asp	Phe	Xaa	Xaa	Phe	Xaa	Asp	Arg
	210					215						220

<210> 22
<211> 167
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: degenerate
polypeptide sequence

<220>
<221> SITE
<222> 7
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Pro, Phe or Tyr

<220>
<221> SITE
<222> 8
<223> Xaa represents Gly, Ala, Val, Leu or Ile

<220>
<221> SITE
<222> 9
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Lys, His or Arg

<220>
<221> SITE
<222> 12
<223> Xaa represents Lys, Arg or His

<220>
<221> SITE
<222> 13
<223> Xaa represents Phe, Trp, Tyr or an amino acid gap

<220>
<221> SITE
<222> 14
<223> Xaa represents Gly, Ala, Val, Leu, Ile or an amino acid gap

<220>
<221> SITE
<222> 17
<223> Xaa represents Asn, Gln, His, Arg or Lys

<220>
<221> SITE
<222> 19
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> SITE
<222> 22
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>

<221> SITE
<222> 27
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> SITE
<222> 29
<223> Xaa represents Ser, Thr, Gln or Asn

<220>
<221> SITE
<222> 30
<223> Xaa represents Met, Cys, Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> SITE
<222> 31
<223> Xaa represents Gly, Ala, Val, Leu, Ile or Pro

<220>
<221> SITE
<222> 33
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 40
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Pro, Arg, His or Lys

<220>
<221> SITE
<222> 41
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Phe or Tyr

<220>
<221> SITE
<222> 44
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 45
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> SITE
<222> 46
<223> Xaa represents Thr or Ser

<220>
<221> SITE
<222> 48
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Asn or Gln

<220>
<221> SITE
<222> 53

<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 54
<223> Xaa represents Asp or Glu

<220>
<221> SITE
<222> 71
<223> Xaa represents Ser or Thr

<220>
<221> SITE
<222> 79
<223> Xaa represents Glu, Asp, Gln or Asn

<220>
<221> SITE
<222> 83
<223> Xaa represents Glu or Asp;

<220>
<221> SITE
<222> 84
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 85
<223> Xaa represents Gly, Ala, Val, Leu or Ile

<220>
<221> SITE
<222> 87
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
<221> SITE
<222> 95
<223> Xaa represents Met, Cys, Gln, Asn, Arg, Lys or His

<220>
<221> SITE
<222> 100
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 107
<223> Xaa represents Trp, Phe, Tyr, Arg, His or Lys

<220>
<221> SITE
<222> 114
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser, Thr, Tyr or Phe

<220>
<221> SITE
<222> 115
<223> Xaa represents Gln, Asn, Asp or Glu

<220>
<221> SITE
<222> 116
<223> Xaa represents Asp or Glu;

<220>
<221> SITE
<222> 125
<223> Xaa represents Gly, Ala, Val, Leu, or Ile

<220>
<221> SITE
<222> 134
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 135
<223> Xaa represents Asn, Gln, Thr or Ser

<220>
<221> SITE
<222> 139
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser, Thr, Met or Cys

<220>
<221> SITE
<222> 141
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
<221> SITE
<222> 157
<223> Xaa represents Arg, His or Lys

<220>
<221> SITE
<222> 158
<223> Xaa represents Asn, Gln, Gly, Ala, Val, Leu or Ile

<220>
<221> SITE
<222> 160
<223> Xaa represents Gly, Ala, Val, Leu or Ile

<220>
<221> SITE
<222> 162
<223> Xaa represents Gly, Ala, Val, Leu, Ile, Ser, Thr or Cys

<220>
<221> SITE

<222> 166
 <223> Xaa represents Gly, Ala, Val, Leu, Ile, Thr or Ser

<220>
 <221> SITE
 <222> 167
 <223> Xaa represents Asp or Glu.

<400> 22
 Cys Gly Pro Gly Arg Gly Xaa Xaa Xaa Arg Arg Xaa Xaa Xaa Pro Lys
 1 5 10 15
 Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
 20 25 30
 Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
 35 40 45
 Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
 50 55 60
 Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg
 65 70 75 80
 Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp
 85 90 95
 Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His
 100 105 110
 His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr
 115 120 125
 Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala
 130 135 140
 Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa
 145 150 155 160
 His Xaa Ser Val Lys Xaa Xaa
 165

<210> 23
 <211> 74
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: primer

<400> 23
 gcgcgcttcg aagcgaggca gccagcgagg gagagagcga gcgggagcgc cggagcgagg 60
 aaatcgatgc gcgc

<210> 24
<211> 74
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 24
gcgcgcagat ctgggaaagc gcaagagaga gcgcacacgc acacacccgc cgcgcgact 60
cgggatccgc gcgc 74

<210> 25
<211> 996
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: gene
activation construct

<400> 25
cgaagcgagg cagccagcga gggagagagc gagcgggcga gccggagcga ggaaatcgaa 60
ggttcgaatc cttccccac caccatcact ttcaaaagtc cgaaagaatc tgctccctgc 120
ttgtgtgttg gaggtcgctg agtagtgcg gcgtaaaatt taagctacaa caaggcaagg 180
cttgaccgac aattgcatga agaatctgct taggggttagg cgttttgcgc tgcttcgcga 240
tgtacggggc agatatacgc gttgacattg attattgact agttattaat agtaatcaat 300
tacgggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa 360
tgggccgcct ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt 420
tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggact atttacggta 480
aactgccac ttggcagtac atcaagtga tcatatgcca agtacgcccc ctattgacgt 540
caatgacggt aaatggcccc cctggcatta tgcccagtac atgaccttat gggactttcc 600
tacttggcag tacatctacg tattagtcac cgctattacc atgggtgatgc ggttttggca 660
gtacatcaat gggcgtggat agcggtttga ctcacgggga tttccaagtc tccaccccat 720
tgacgtcaat gggagtttgt tttggcacca aaatcaacgg gactttccaa aatgtcgtaa 780
caactccgcc ccattgacgc aaatgggcgg taggcgtgta cgggtgggagg tctatataag 840
cagagctctc tggctaacta gagaaccac tgcttactgg cttatcgaaa ttaatacgac 900
tcactatagg gagaccaag cttggtaccg agctcggatc gatctgggaa agcgcaagag 960

agagcgcaca cgcacacacc cgccgcgcgc actcgg

996

<210> 26

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: antisense
construct

<400> 26

gtcctggcgc cgccgccgcc gtcgcc

26

<210> 27

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: antisense
construct

<400> 27

ttccgatgac cggcctttcg cggatga

26

<210> 28

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: antisense
construct

<400> 28

gtgcacggaa aggtgcaggc cacact

26

cnt
B₁